

Applicants have noted several additional minor typographic errors which should be corrected. These additional amendments refer to page numbers in the application as filed.

In the Specification:

Please amend the specification at page 18 to replace the paragraph at lines 3-19 with the following:

B1

-- Multivalent ligands of this invention can be used to modulate signal transduction in prokaryotic and eukaryotic organisms. The ligands function in a variety of signal transduction processes. Prokaryotes have a highly conserved intracellular signal transduction system, the two component system. The major components of this system are varying numbers of alternating histidine-aspartic acid kinase-mediated phosphorylation events, such as virulence, antibiotic resistance, response to environmental stress and sensing. The components of the two component system are highly conserved in prokaryotes. In contrast, eukaryotes appear to have very few two component systems for signal transduction. This orthogonality makes the two component signaling pathway a prime target for exploitation in therapeutic design for the control of bacterial infection. Major signal transduction systems in eukaryotes are mediated by G-protein-linked receptors and enzyme-linked receptors (including receptor guanylyl cyclases, receptor tyrosine kinases, tyrosine-kinase-associated receptors, receptor tyrosine phosphatases, and receptor serine/threonine kinases). The ability to modulate or regulate signal transduction in these pathways allows control over a wide variety of biological processes in eukaryotic cells and eukaryotic organisms (including mammals and specifically humans) and provides significant opportunity for the design of therapeutics. --

2 Please replace the paragraph on page 22, lines 10-18 with the following:

B2

-- RE is a recognition element as discussed above that can be any of a variety of chemical or biochemical species that are recognized by and which selectively bind to cell

B2
cont

receptors, particularly, transmembrane receptors and cell surface receptors. SRE is a signal recognition element as discussed above that can be any of a variety of chemical or biochemical species that are recognized by one or more cells and which induce a biological response by the cell; "L" is an optional linker group that can provide functional groups for covalent bonding of the RE, SRE or FE to the polymer (oligomer) backbone. FE is a chemical or biochemical functional group other than an SRE, as discussed above. Other examples of ROMP scaffolds are illustrated in Schemes 2 and 3.-

On pages 23-24 in the paragraph bridging the pages, please rewrite the paragraph as follows:

B3

-- The linker can provide for spacing of the RE, SRE or FE group(s) from the backbone or can provide for structural flexibility. Linkers may be the same or different on different monomers in the polymer. Linkers that are used in a monomeric scaffold to bond to RE, SRE or FE can also be all the same or different. In a given multivalent ligand carrying one type of RE or SRE group, the linker is preferably the same throughout the polymer. Linkers are generally selected so that they are compatible with the intended application of the multivalent ligand and to avoid interference with the function of signal groups. The linker is preferably linear and preferably ranges in length from 1 to about 20 atoms. The linker may contain alicyclic groups (such as a cyclohexyl group). The linker can be an alkyl chain carrying functional groups for bonding to the backbone of the ligand and to the signal. The linker can also be an ether, ester, ketone, amine, amide or thioether chain. In a specific embodiment, the linker can be described as an linear alkyl chain having from 1 to about 20 carbon atoms in length in which one or more non-neighboring CH₂ groups are optionally replaced with an -O-, -S-, -NH-, -NR¹⁰-, -CO-, -NH-CO-, -O-CO-, -HC=HC-, or -C≡C- group, where R¹⁰ is an alkyl or aryl group. Linker CH₂ groups can be substituted with halogens, alkoxy, or alkyl groups. In the absence of a linker group, the ROMP backbone or the signal group itself must provide the functionality for covalent bonding of the signal to the backbone. Exemplary linkers include those illustrated in Scheme 3.--

On pages 44-45, please replace the paragraph bridging the pages with the following:

34
--Further experiments were conducted which demonstrated that ConA-mediated agglutination of erythrocytes could be controlled by addition of multivalent ligands (compounds 9-13). Certain combinations of ConA and multivalent ligands exhibited enhanced agglutination of these cells compared to ConA itself, as shown in Fig. 11. In particular, a combination of ConA tetramer and multivalent ligand (compound 13) at concentration ratio 10:1 (based on tetrameric ConA and based on the number of mannose residues) exhibited significantly enhanced agglutination compared to ConA alone.--

In the Claims:

2 Please replace claim 100 as follows:

35
--100. The multivalent ligand of claim 99 wherein the FE in the at least one L²-FE group in the ligand is a detectable label or a reporter group.—

REMARKS

This supplement to the preliminary amendment corrects inadvertent errors in the replacement sheets provided with the preliminary amendment and response to the Notice of Missing Parts filed July 27, 2001. Corrected replacement sheets for pages 10, 13, 18, and 79 are submitted herewith. The corrections made to the replacement sheets are obvious on review of the preliminary amendment that was submitted.

This submission also requests amendment of several additional clerical errors in the specification and claims as filed which were previously overlooked. These new amendments correct spelling errors and on page 24 corrects the incorrect formula of a chemical group replacing -C=C- which represents an ethylene group with the correct formula: -HC=CH-. All of the amendments made represent obvious corrections to obvious errors in the specification and claims.